CLAIMS

WHAT IS CLAIMED IS:

1. A method for determining the effectiveness of a therapeutic regimen for the treatment of a cancer in a subject, the method comprising:

(a) determining a genomic polymorphism in the subject with said cancer; and

(b) concluding that the therapeutic regimen will be effective if the genomic polymorphism exhibited by the subject is of a certain type.

2. The method of claim 1 wherein the therapeutic regimen comprises administering a chemotherapeutic drug to the subject.

3. The method of claim 2 wherein the chemotherapeutic drug is a TS directed drug.

4. The method of claim 3 wherein the TS directed drug is a fluropyrimidine.

5. The method of claim 4 wherein the fluoropyrimidine is 5-fluorouracil.

6. The method of claim 5 wherein the subject is a human subject.

7. The method of claim 6 wherein determining the genomic polymorphism of the subject comprises determining the subject's genotype at a tandemly repeated 28 base pair sequence in the thymidilate synthase gene's 5' UTR whereby the subject will exhibit the poorest response to administration of 5-fluorouracil if the subject's genotype is homozygous for a triple repeat of the tandemly repeated sequence, a less poor response to administration of 5-fluorouracil if the subject's genotype is heterozygous for a double repeat and a triple repeat of the tandemly repeated sequence, and the best response to administration of 5-fluorouracil if the subject's genotype is homozygous for a double repeat of the tandemly repeated sequence.

8. The method of claim 6 wherein determining the subject's genotype further comprises:

extracting genomic DNA from a biological sample of the subject;

amplifying the 5' UTR of the thymidilate synthase gene of said genomic DNA using

polymerase chain reaction; and

analyzing the polymerase chain reaction product to determine the subject's genotype.

9. The method of claim 8 wherein analysis of the polymerase chain reaction product is performed using electrophoresis.

10. The method of claim 1 wherein the cancer is breast cancer.

11. The method of claim 1 wherein the cancer is colorectal cancer.

12. The method of claim 1 wherein the cancer is gastric cancer.

13. The method of claim 1 wherein the cancer is esophageal cancer

14. The method of claim 1 wherein the cancer is Burkitt's lymphoma.

15. The method of claim 1 wherein the cancer is B follicular cell lymphoma.

16. The method of claim 1 wherein the cancer is small cell lung carcinoma.

17. A method for predicting the effect of a therapeutic regimen for treating a cancer in a human subject wherein a chemotherapeutic drug is administered to the human, the method comprising:

associating a genomic polymorphism of the human subject with intratumoral expression of a gene wherein said gene expression influences the efficacy of said therapeutic regimen.

18. The method of claim 17 wherein the chemotherapeutic drug is a TS directed drug.

19. The method of claim 18 wherein the gene is thymidilate synthase gene.

20. The method of claim 19 wherein the genomic polymorphism of the human subject is the subject's genotype at a tandemly repeated 28 base pair sequence in the thymidilate synthase gene 5' UTR.

21. The method of claim 20 wherein the therapeutic regimen is most effective if the subject's genotype is homozygous for a double repeat of the tandemly repeated sequence, is less effective if the subject's genotype is heterozygous for a double and a triple repeat of the tandemly repeated sequence and is least effective if the subject's genotype is homozygous for a triple repeat of the tandemly repeated sequence.

22. A method for determining the expression level of a gene in cells of a subject, the method comprising:
determining a genomic polymorphism of the subject; and
associating the expression level of said gene with said genomic polymorphism.

23. The method of claim 22 wherein the gene is thymidilate synthase gene.

24. The method of claim 23 wherein the genomic polymorphism of the subject is the subject's genotype at a tandemly repeated 28 base pair sequence in the thymidilate synthase gene's 5' UTR.

25. The method of claim 24 wherein the expression level of said gene is highest if the subject's genotype is homozygous for a triple repeat of the tandemly repeated sequence, is less if the subject's genotype is heterozygous for a double and a triple repeat of the tandemly repeated sequence and is least if the subject's genotype is homozygous for a double repeat of the tandemly repeated sequence.

26. A method for determining the effectiveness of a chemotherapeutic regimen wherein a TS directed drug is administered to a human subject, the method comprising:
determining the subject's genotype at a tandemly repeated 28 base pair sequence in the thymidilate synthase gene's 5' UTR whereby the subject will exhibit the poorest response to administration of the TS directed drug if the subject's genotype is homozygous for a triple repeat of the tandemly repeated sequence, a less poor response to administration of the TS directed drug if the subject's genotype is heterozygous for a double repeat and a triple repeat of the tandemly repeated sequence, and the best response to administration of the TS directed drug if the subject's genotype is homozygous for a double repeat of the tandemly repeated sequence.

27. The method of claim 26 wherein the TS directed drug is a fluoropyrimidine.

28. The method of claim 27 wherein the fluoropyrimidine is 5-fluorouracil.

29. A method for determining an appropriate chemotherapeutic regimen to treat a cancer in a subject, the method comprising:
associating a genomic polymorphism of the subject with the effectiveness of a chemotherapeutic regimen.

30. The method of claim 29 wherein the method is used to select or reject a chemotherapeutic drug to treat the cancer.

31. A kit for use in screening for the effectiveness of TS directed drug therapy in human subjects.

32. The kit of claim 31 comprising:
all or some of the positive controls, negative controls, reagents, primers, sequencing markers, probes and antibodies for determining the presence or absence of the tandemly repeated 28 base-pair nucleic acid sequence that defines the genomic polymorphism in the 5' UTR of the TS gene.

33. The kit of claim 31 wherein the kit components may be provided in solution or as a liquid dispersion or the like.

34. The kit of claim 31 comprising DNA tandemly repeated sequences that determine the type of genomic polymorphism of the TS gene in Tris-EDTA buffer solution preferably kept at 4 °C.

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